The use of Argentum-Quartz® solution in primary or recurrent perianal fistulas: first experience on three cases

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Abstract

Primary perianal fistulous pathology represents a painful condition often noticeable in patients affected by Crohn’s disease or Ulcerative colitis. It causes difficult defecation and can evolve in perianal abscess that should be urgently ascertained and drained. The present work aims to propose Argentum-Quartz® as valid non-surgical therapeutic treatment in order to reach a more comfortable perianal fistula healing. In fact, our preliminary data allow us to consider Argentum Quartz® ideally employable for treatment of perianal fistulas associated or not with IBDs, representing a reliable sphincter-sparing solution.

Key words: argentum/quartz solution, cryptitis, perianal suppurative fistulas, seton

Background

Patients with Inflammatory Bowel Diseases (IBDs), such as Crohn’s Disease (CD), Ulcerative Colitis (UC) and Indeterminate Colitis, often undergo pyogenic, suppurative, complications. Actually, the main cause of these complications could be recognized in the characteristic inflammation of the mucosal compartment, which could favour the onset of pyogenic infections. In particular, the infection of Lieberkuhn’s recto-anal glands usually represents the “primum movens” for the onset of suppurative fistulas. The contact of Enteropathogenic bacteria with the anal crypts worsen mucosal inflammation, favouring penetration of pyogenic flora in adipose-sphincteric deep tissues and perirectal abscess formation (1). Histological studies performed on biopic specimens harvested by affected patients, demonstrated that, between the internal and external anal sphincter, there is a substantial aggregation of glands, greatly affected by the inflammatory process (cryptitis). The extension of this process to the surrounding tissues could hesitate in abscess cavity formation and, subsequently, in a frankly purulent fistula.

Secondary fistulas debilitate particularly patients whose own health is already mined by systemic inflammatory response. Pain and difficult defecation are the main complaints. The presence of a perianal abscess should be ascertained and, if present, should be drained urgently (2). Current management of fistula, mostly provides surgical approaches (3). Fistula flattening and fistulectomy represent the more conservative approaches. In cases of sphincter involvement, the use of setone creates a great discomfort for the patient and increases the time of healing. Recently, less invasive and more conservative treatments were taken in consideration as valid alternatives to surgery in order to preserve the integrity of the anatomical structures. Fibrin glue employment stimulates tissue repair capacity and represent the most representative example (4,5). Studies conducted on murine perianal tissue investigated the effect of Argentum-Quartz® (WALA Italia srl, Milan, Italy) and revealed its ability in stimulating the proliferation of fibroblasts and favouring tissue repair (6,7). The Argentum-Quartz® solution synergistically leverages the antiseptic properties of the silver and those fibro-reparative of the quartz (8). These properties are universally recognized and reported in various works from literature (9-11). The administration of Argentum-Quartz® guarantee antiseptic activity against pyogenic and Enteropathogenic bacteria, inducing attenuation of mucosal inflammation, stimulating fibroblast activity and leading to a “fully recovered” tissue. Starting from this assumption, the presented study evaluated the effects of Argentum-Quartz® topical instillation in perianal fistulas (both primary and recurrent), in the attempt to find a valid alternative to surgical practices.
Material and methods

In this perspective cohort study, three patients with simple intersphincteric and extrasphincteric fistulas were enrolled (see Table 1).

One of the enrolled subjects suffered from Crohn’s disease (diagnosed endoscopically, histologically and radiologically) and one patient underwent fistulotomy one year before. Subjects with complex fistulas were excluded from the study. Complex fistulas were defined as deep trans-sphincteric fistulas, supralever fistula, fistulas with associated abscess formation or secondary tracks, anovaginal fistulas or horseshoe fistulas. An informed consent was obtained from all patients prior to their inclusion. All procedures were performed in accordance with the Declaration of Helsinki ethical standards.

Before the procedure, each fistula was correctly assessed thanks to transanal ultrasonography, using a 10-13 MHz 3D rotating endoprobe (Fig. 1).

After the cutaneous area adjacent to fistula opening was sterilized with povidone iodine and hair were removed, a 20 G x 1.26 inches catheter (1.1 mm x 32 mm) was inserted into the passage (Fig. 2) and 1 mL Argentum-Quartz® solution was injected.

The treatment consisted of twice a week administration of Argentum-Quartz® solution for 4 weeks, followed by a pause of 8 days and other 4 weeks of treatment (16 administrations). After treatment completion, all patients were monitored for 4 months, not only clinically, but also evaluating disease evolution by means of ultrasounds. A questionnaire was administered after 3 months, in order to evaluate patient satisfaction grade (on a 1 to 5 scale). The failure of procedure was defined as the occurrence of at least one of the following: abscess, purulent discharge, visible external opening or further drainage procedure.

Results

As showed in table 1, four months after the end of treatment, two of the three enrolled patients showed a complete fistula closure. One of them, submitted to fistulotomy one year before, benefited from the therapy, showing a complete closure only after 4 weeks (Figg. 3 and 4).

Table 1. Fistula classification and related clinical outcome

<table>
<thead>
<tr>
<th>Patients demographic characteristics</th>
<th>Fistula classification (based on Park’s criteria)</th>
<th>Clinical outcome (4 months after surgery)</th>
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<tbody>
<tr>
<td>Age 42 Male</td>
<td>Extrasphincteric fistula</td>
<td>Complete closure*</td>
</tr>
<tr>
<td>Age 60 Male</td>
<td>Intersphincteric fistula</td>
<td>Partial closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No suppurative phenomena at follow-up</td>
</tr>
<tr>
<td>Age 29 Male</td>
<td>Extrasphincteric fistula</td>
<td>Complete closure</td>
</tr>
</tbody>
</table>

*Patient treated for relapse of perianal fistula who underwent surgery the year before
Ultrasonography confirmed the complete closure, appearing inactive fistulas as tubular fibrotic bands without fluid content (Fig. 5).

During observation period, the third patient, with an interspincteric fistula, had an exacerbation of Crohn’s Disease. The patient complained of abdominal colic pain and diarrhoea. In this case, a contextual treatment with oral mesalazine 800 mg three times daily and cortisone (prednisone 25 mg, 1 tablet/day) for 20 days, was established. After therapy, Crohn disease symptoms vanished and Argentum-Quartz® treatment allowed an almost complete fistula closure, with no suppurrative complications. Satisfaction assessment showed high values for all three patient (only the patient with partial closure marked with “4” its satisfaction).

Discussion

Currently, surgery does not represent a resolutive procedure in anal fistula treatment, due to fistula recurrence, after months or years. Only broad conclusions can be drawn by reviewing literature. Setons provide palliation and can be used in the long term; advancement flap and stem cell therapy may emerge as effective therapies, but require well designed randomized trials. A number of other procedures including ligation of interspincteric fistula tract (LIFT), video-assisted anal fistula treatment (VAAFT) and over-the-scope clip (OTSC®) require further evaluation. Therefore, patients willingly accepts to undergo alternative treatments, in an attempt to avoid surgical procedures. Unfortunately, fibrin glue has largely fallen out of favour, and fistula plugs are considered to have limitations, including failure and associated sepsis. Advancement flaps may not be technically possible with a ‘woody’ rectum, extensive fibrosis or active proctitis. The combination of recurrent Crohn’s disease and loose stool means that any sphincter disruption or alteration in anocutaneous sensation may have an exaggerated impact on continence. Clinicians and patients may therefore understandably be keen to avoid procedures that pose additional risk to the sphincter, including fistulotomy.

The present work represents an experimental study prompted to validate the efficacy of Argentum-Quartz® as valid non-surgical, sphincter-sparing treatment, in order to reach a more comfortable, both for the patient and for the surgeon, perianal fistula healing. In our small case series, only one case of incomplete closure was registered, demonstrating how Argentum-Quartz® could be useful in preventing the onset of inflammatory suppurative events. In fistulas secondary to Crohn’s disease, partial healing may be due to the well-known higher complexity of interspincteric rather than extraspincteric fistula treatment or to the need for longer treatment and follow-up. In Crohn’s disease, the auto-resolution capacity of the inflammatory process is very limited. The resulting tissue framework is characterized by an infiltrate of neutrophils and related cytotoxic and cytodestructive enzymes together with oxygen free radicals. The latter, induce active tissue necrosis not balanced by efficient reparative processes. The further presence of a
mixed bacterial flora, composed of aerobic pathogens, such as Escherichia coli, Proteus vulgaris, Staphylococcus aureus, and Streptococcus species, and anaerobic organisms, such as Bacteroides and Peptostreptococcus, contribute to perianal tissue disruption and chronicity (13,14). As reported by Fayaz et al., silver nanoparticles can synergistically cooperate with antibiotics for the production of collagen fibres, favouring tissue healing (8,9). The mechanism responsible for this therapeutic effect seems to reside into the capacity of silver nanoparticles of inhibiting the action of special cyto-detrimental peptidoglycan and cellular DNA damage (10). Moreover, nanoparticles reduce levels of acute phase proteins such as hemopexina, the haptoglobin and serum amyloid protein (SAP). In literature, the use of preparations based on silver has been already tested on murine models of pulmonary diseases and has been employed for the treatment of tracheo-bronchial fistulas (15-17).

The double action of Argentum-Quartz solution, one directed against chronic inflammation and the other against enteropathogenic bacteria, stimulates proliferation and differentiation of fibroblasts and favour reparative processes. For this reason, the presented treatment could be considered a useful, non surgical, therapeutic approach to treat anorectal fistulas.

Conclusions

Argentum-Quartz® solution revealed a good therapeutic alternative to classical surgical approaches resulting also compatible with the concomitant administration of anti-inflammatory drugs employed in IBDs treatment. The positive results obtained prompt us to encourage us to move forward increasing both number of patients to enroll and follow-up period. Furthermore, these preliminary data led us to consider Argentum-Quartz® as a sphincter-sparing solution, ideally employable for treatment of perianal fistulas associated or not with IBDs. We do not know how these encouraging results obtained with Argentum-Quartz® conservative treatment are long lasting. Therefore, we would need for longer follow up to assess the effectiveness of this non-invasive procedure in the long period. Finally, we aim to continue the study enrolling a larger cohort of patients for observing them for a longer follow-up period.

References

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